

Claims

What is claimed is:

1. A method of magnetic resonance investigation of a sample, preferably of a human or non-human animal body, said method comprising:

(i) nuclear spin polarising a solid MR imaging agent (i.e. a material containing in its molecular structure a non-zero nuclear spin nucleus) by

(a) spin refrigeration, or by,

(b) irradiating with circularly polarised light;

(ii) administering the nuclear spin polarised MR imaging agent to said sample, preferably after dissolution in a physiologically tolerable solvent and also preferably after separation from some or all of the paramagnetic species or chromophores;

(iii) exposing said sample to a radiation at a frequency selected to excite nuclear spin transitions in selected nuclei therein, e.g. the spin polarised nuclei of the MR imaging agent;

(iv) detecting magnetic resonance signals from said sample; and

(v) optionally generating an image, dynamic flow data, diffusion data, perfusion data, physiological data (e.g. pH, pO₂, pCO₂, temperature or ionic concentrations) or metabolic data from said detected signals.

2. A method as claimed in claim 1 wherein said agent is administered to said sample after dissolution in water.

3. A method as claimed in either one of claims 1 and 2 wherein said agent further comprises other pharmaceutical additives.

4. A method as claimed in any one of the preceding claims wherein said solid MR imaging agent is a water-soluble high T_1 agent.

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5. A method as claimed in any one of the preceding claims wherein said MR imaging agent retains its polarisation when transported in a substantially uniform magnetic field and at low temperature.

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6. A method as claimed in claim 5 wherein said magnetic field is greater than 10 mT.

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7. A method as claimed in claim 5 wherein said magnetic field is greater than 1T.

8. A method as claimed in any one of claims 5 to 7 wherein said temperature is lower than 80K.

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9. A method as claimed in any one of claims 5 to 7 wherein said temperature is lower than 4.2K.

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10. A method as claimed in any one of the preceding claims wherein the solution formed retains its polarisation in frozen form.

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11. A method as claimed in any one of the preceding claims wherein a magnetic field is present during the dissolution stage.

12. A method as claimed in any one of the preceding claims wherein step (i) comprises:

i) irradiating a solid compound having a singlet electronic ground state and containing a non zero nuclear spin nucleus with light to generate an excited polarized triplet electronic state of said agent;

5 ii) transforming electronic polarization of said solid compound into a nuclear spin polarization in a soluble solid MR imaging agent to form a nuclear spin polarised MR imaging agent;

10 iii) dissolving said polarised MR imaging agent in an aqueous medium.

13. Use of a paramagnetic substance for the manufacture of an MR imaging composition for use in a method of diagnosis involving generation of an MR image by MR imaging of a human or non-human animal body, wherein manufacture of said composition
15 involves spin refrigeration nuclear spin polarisation of said MR imaging agent.

14. Use of an MR imaging agent for the manufacture of an MR imaging composition for use in a method of diagnosis involving
20 generation of an MR image by MR imaging of a human or non-human animal body, wherein manufacture of said composition involves spin refrigeration nuclear spin polarisation of said MR imaging agent.

25 15. An MR imaging composition comprising a solution of a spin refrigerator nuclear spin polarised MR imaging agent in a physiologically tolerable solvent, optionally together with one or more physiologically tolerable excipients.

30 16. An apparatus for use in the method as claimed in claim 1 when the polarising of a MR imaging agent is by spin refrigeration, the apparatus comprising:

i) a chamber cooled to a temperature preferably lower than 80K disposed in the primary magnetic field of MR apparatus, or in a separate magnetic field, of strength 0.2T or more;

and wherein said chamber is:

5 i) adapted to receive particulate solid MR imaging agent, doped with or intimately mixed with paramagnetic polarising agent;

10 ii) rotates said agent about an axis non-parallel with the primary field or passes said agent through a conduit such that it rotates in that way or mixes said agent such that it rotates in that way, or (where the chamber is in a separate magnetic field) rotates the magnetic field about one or more axes;

15 iii) dissolves said polarised solid agent in or passes it to a mixing chamber, where it is dissolved in a physiologically tolerable solvent;

iv) passes the solution thus formed through or over an immobilised paramagnetic metal binding agent and/or through a filter;

20 v) and into the conduit for administration into a sample situated within the primary magnetic field of the MR imager.

17. An apparatus as claimed in claim 16 wherein said chamber is cooled to lower than or equal to 1K.

25 18. An apparatus as claimed in either one of claims 16 and 17 wherein the strength of said magnetic field is 0.5 to 10T.

30 19. A process for the preparation of a nuclear spin polarised MR imaging agent, said process comprising irradiating a solid compound having a singlet electronic ground state and containing a non zero nuclear spin nucleus with light to

generate an excited polarized triplet electronic state of said agent;

transforming electronic polarization of said solid compound into a nuclear spin polarization in a soluble solid MR imaging agent to form a nuclear spin polarised MR imaging agent, optionally dissolving said MR imaging agent in an aqueous medium (preferably a physiologically tolerable medium), and optionally storing said polarised MR imaging agent at a reduced temperature and at a magnetic field of greater than 10 mT.

20. A process as claimed in claim 19 wherein said reduced temperature is liquid nitrogen temperature or below.

21. A process as claimed in claim 19 wherein said reduced temperature is liquid helium temperature.

22. A process as claimed in any one of claims 19 to 21 wherein said magnetic field is greater than 2T.

23. A process for the preparation of a polarised electronic triplet state of a solid compound having a singlet electronic ground state said process comprising irradiating said compound in a solid state with a first radiation of a wavelength selected to excite said compound from a ground singlet electronic state to an excited singlet electronic state and with a positively or negatively, circularly polarised second radiation of a wavelength selected to excite said compound from the lowest triplet electronic state to the next-to-lowest triplet electronic state.

24. A process as claimed in claim 23 wherein said compound is a water-soluble compound containing at least one non-zero nuclear spin nucleus.

25. Use of a water-soluble, heterocyclic chromophore-containing compound containing an $I=\frac{1}{2}$ nucleus for the manufacture of an MR imaging composition for use in a method of diagnosis involving generation of an MR image by MR imaging of a human or non-human animal body, said manufacture comprising nuclear spin polarisation of said compound in the solid state and dissolution of the nuclear spin polarised compound in an aqueous medium.

26. Use as claimed in claim 25 wherein said $I=\frac{1}{2}$ nucleus is ^{13}C or ^{15}N .

27. A water-soluble MR imaging agent compound:

- (i) containing a nuclear spin polarised $I=\frac{1}{2}$ nucleus;
- (ii) having a molecular weight below 1000D;
- (iii) containing a cyclic chromophore; and
- (iv) having an nmr spectrum for said $I=\frac{1}{2}$ nucleus having a linewidth of less than 100 Hz.

28. An agent compound as claimed in claim 27 wherein said molecular weight is below 500D.

29. An agent as claimed in either one of claims 27 and 28 wherein said cyclic chromophore is heterocyclic.

30. An agent as claimed in any one of claims 27 to 29 wherein said linewidth is below 1 Hz.

FIGURE 11-1501

31. A physiologically tolerable MR imaging composition comprising a physiologically tolerable nuclear spin polarised MR imaging agent as claimed in any one of claims 27 to 30 dissolved in water together with one or more physiologically tolerable excipients, said imaging agent containing nuclei of a $I=\frac{1}{2}$ isotope characterised in that said nuclei are polarised such that their nmr signal intensity is equivalent to a signal intensity achievable in a magnetic field of at least 0.1T.

32. A composition as claimed in claim 31 wherein said nuclei are at higher than natural abundance.

33. A composition as claimed in either one of claims 31 and 32 wherein said magnetic field is at least 450T.

34. A composition as claimed in any one of claims 31 to 33 wherein said composition is sterile and is stable at a physiological temperature.

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